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☐ 1. Document ID: US 6180379 B1

L3: Entry 1 of 2

File: USPT

Jan 30, 2001

US-PAT-NO: 6180379

DOCUMENT-IDENTIFIER: US 6180379 B1

TITLE: Cyclin-selective ubiquitin carrier polypeptides

DATE-ISSUED: January 30, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ruderman; Joan V.	Wellesley	MA	N/A	N/A
Hershko; Avram	Haifa	N/A	N/A	ILX
Kirschner; Marc W.	Newton	MA	N/A	N/A
Townsley; Fiona	Somerville	MA	N/A	N/A
Aristarkov; Alexander	Boston	MA	N/A	N/A
Eytan; Esther	Haifa	N/A	N/A	ILX
Yu; Hongtao	Somerville	MA	N/A	N/A

US-CL-CURRENT: 435/193; 435/68.1, 530/350

ABSTRACT:

Disclosed are novel human and clam ubiquitin carrier polypeptides involved in the ubiquitination of cyclins A and/or B. Also disclosed are inhibitors of such polypeptides, nucleic acids encoding such polypeptides and inhibitors, antibodies specific for such polypeptides, and methods of their use.

16 Claims, 28 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 19

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMMC	Draw Desc	Image
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☐ 2. Document ID: US 5726025 A

L3: Entry 2 of 2

File: USPT

Mar 10, 1998

US-PAT-NO: 5726025
DOCUMENT-IDENTIFIER: US 5726025 A

TITLE: Assay and reagents for detecting inhibitors of ubiquitin-dependent degradation of cell cycle regulatory proteins

DATE-ISSUED: March 10, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kirschner; Marc W.	Newton	MA	N/A	N/A
King; Randall W.	Brookline	MA	N/A	N/A
Peters; Jan-Michael	Brookline	MA	N/A	N/A

US-CL-CURRENT: 435/7.2; 435/15, 435/7.23, 435/7.7, 435/7.9, 436/503, 436/86

ABSTRACT:

The present invention provides a systematic and practical approach for the identification of candidate agents able to inhibit ubiquitin-mediated degradation of a cell-cycle regulatory protein, such as cyclins. One aspect of the present invention relates to a method for identifying an inhibitor of ubiquitin-mediated proteolysis of a cell-cycle regulatory protein by (i) providing a ubiquitin-conjugating system that includes the regulatory protein and ubiquitin under conditions which promote the ubiquitination of the target protein, and (ii) measuring the level of ubiquitination of the subject protein brought about by the system in the presence and absence of a candidate agent. A decrease in the level of ubiquitin conjugation is indicative of an inhibitory activity for the candidate agent. The level of ubiquitination of the regulatory protein can be measured by determining the actual concentration of protein:ubiquitin conjugates formed; or inferred by detecting some other quality of the subject protein affected by ubiquitination, including the proteolytic degradation of the protein.

30 Claims, 2 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KVMC	Draw Desc	Image
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Search Results - Record(s) 1 through 3 of 3 returned.

☒ 1. Document ID: US 6232081 B1

L4: Entry 1 of 3

File: USPT

May 15, 2001

US-PAT-NO: 6232081

DOCUMENT-IDENTIFIER: US 6232081 B1

TITLE: Method for the detection of NF-.kappa.B regulatory factors

DATE-ISSUED: May 15, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Harper; Jeffrey Wade	Sugarland	TX	N/A	N/A
Elledge; Stephen J.	Houston	TX	N/A	N/A
Winston; Jeffrey T.	Sugar Land	TX	N/A	N/A

US-CL-CURRENT: 435/7.1; 435/7.2, 436/501, 436/516, 436/536

ABSTRACT:

The present invention provides compositions and methods for gene identification, as well as drug discovery and assessment. In particular, the present invention provides components of an E3 complex involved in ubiquitination of cell cycle regulators and other proteins, as well as members of a class of proteins that directly function in recognition of ubiquitination targets. The present invention also provides sequences of multiple F-box proteins.

4 Claims, 33 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 15

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KVMC	Draw Desc	Image
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☐ 2. Document ID: US 6180379 B1

L4: Entry 2 of 3

File: USPT

Jan 30, 2001

US-PAT-NO: 6180379

DOCUMENT-IDENTIFIER: US 6180379 B1

TITLE: Cyclin-selective ubiquitin carrier polypeptides

DATE-ISSUED: January 30, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ruderman; Joan V.	Wellesley	MA	N/A	N/A
Hershko; Avram	Haifa	N/A	N/A	ILX
Kirschner; Marc W.	Newton	MA	N/A	N/A
Townsley; Fiona	Somerville	MA	N/A	N/A
Aristarkov; Alexander	Boston	MA	N/A	N/A
Eytan; Esther	Haifa	N/A	N/A	ILX
Yu; Hongtao	Somerville	MA	N/A	N/A

US-CL-CURRENT: 435/193; 435/68.1, 530/350

ABSTRACT:

Disclosed are novel human and clam ubiquitin carrier polypeptides involved in the ubiquitination of cyclins A and/or B. Also disclosed are inhibitors of such polypeptides, nucleic acids encoding such polypeptides and inhibitors, antibodies specific for such polypeptides, and methods of their use.

16 Claims, 28 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 19

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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☐ 3. Document ID: US 6166293 A

L4: Entry 3 of 3

File: USPT

Dec 26, 2000

US-PAT-NO: 6166293

DOCUMENT-IDENTIFIER: US 6166293 A

TITLE: Method of increasing growth and yield in plants

DATE-ISSUED: December 26, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Doerner; Peter W.	San Diego	CA	N/A	N/A
Lamb; Christopher J.	Edinburgh	N/A	N/A	GBX
Colon-Carmona; Adan	Davis	CA	N/A	N/A

US-CL-CURRENT: 800/290; 435/419, 435/468, 536/23.6, 536/24.1, 800/278, 800/295,
800/298

ABSTRACT:

Provided is a method of producing a genetically modified plant characterized as having increased growth and yield as compared to a corresponding wild-type plant comprising increasing the level of cyclin expression in the plant. The methods include providing a modified nucleic acid regulatory sequence from cycB1a;At resulting in increased gene transcription and expression. Also provided are modified nucleic acid regulatory sequences. Genetically modified plants characterized as having increased growth and yield are also provided.

43 Claims, 6 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image
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Search Results - Record(s) 1 through 6 of 6 returned.☐ 1. Document ID: US 6232081 B1

L10: Entry 1 of 6

File: USPT

May 15, 2001

US-PAT-NO: 6232081

DOCUMENT-IDENTIFIER: US 6232081 B1

TITLE: Method for the detection of NF-.kappa.B regulatory factors

DATE-ISSUED: May 15, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Harper; Jeffrey Wade	Sugarland	TX	N/A	N/A
Elledge; Stephen J.	Houston	TX	N/A	N/A
Winston; Jeffrey T.	Sugar Land	TX	N/A	N/A

US-CL-CURRENT: 435/7.1; 435/7.2, 436/501, 436/516, 436/536

ABSTRACT:

The present invention provides compositions and methods for gene identification, as well as drug discovery and assessment. In particular, the present invention provides components of an E3 complex involved in ubiquitination of cell cycle regulators and other proteins, as well as members of a class of proteins that directly function in recognition of ubiquitination targets. The present invention also provides sequences of multiple F-box proteins.

4 Claims, 33 Drawing figures Exemplary Claim Number: 1
Number of Drawing Sheets: 15

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWMC	Drawl Desc	Image
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☐ 2. Document ID: WO 9934012 A1

L10: Entry 2 of 6

File: EPAB

Jul 8, 1999

PUB-NO: WO009934012A1
DOCUMENT-IDENTIFIER: WO 9934012 A1
TITLE: ASSAYS FOR MODULATORS OF THE INTERACTION BETWEEN ANAPHASE PROMOTING COMPLEX
PROTEIN APC2 AND OTHER APC MEMBERS

PUBN-DATE: July 8, 1999

INVENTOR-INFORMATION:

NAME

JOHNSTON, LELAND HERRIES

COUNTRY

GB

INT-CL (IPC): C12Q 1/02

ABSTRACT:

The present invention relates to the finding of a novel component of the yeast anaphase promoting complex (APC) and its use in assays for inhibitors or modulators of cell cycle progression, particularly in fungal cells. In particular the invention provides an assay for an inhibitor of eukaryotic cell cycle progression which comprises (a) providing a polypeptide which comprises the sequence of the APC2 protein, or a fragment or variant thereof capable of associating with an Anaphase Promoting Complex (APC); (b) providing a second polypeptide member of the APC with which said APC2 protein is capable of forming a complex in the absence of a putative inhibitor; (c) providing a putative inhibitor compound; and (d) measuring the degree of inhibition of binding between (a) and (b) caused by the presence of said putative inhibitor. The second component is preferably APC8 (Cdc23).

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Draw Desc	Image
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☐ 3. Document ID: EP 843008 A1

L10: Entry 3 of 6

File: EPAB

May 20, 1998

PUB-NO: EP000843008A1
DOCUMENT-IDENTIFIER: EP 843008 A1
TITLE: Methods for producing the Anaphase Promoting Complex

PUBN-DATE: May 20, 1998

INVENTOR-INFORMATION:

NAME

NASMYTH, KIM

ZACHARIAE, WOLFGANG

GALOVA, MARTA

COUNTRY

AT

AT

AT

INT-CL (IPC): C12N 15/12; C12Q 1/68; C07K 14/47; C12Q 1/00
EUR-CL (EPC): C07K014/395; C07K014/47

ABSTRACT:

CHG DATE=19990617 STATUS=O> Methods for identifying novel subunits of the human Anaphase Promoting Complex (APC). The subunits may be identified first in yeast cells or directly in human cells and then be used for producing recombinant human APC. Use of recombinant APC in a screening assay to find substances that inhibit rapidly proliferating cells by interfering with the cells' entry into the subsequent cell cycle.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWC	Draw Desc	Image
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☐ 4. Document ID: AU 200040569 A, WO 200058472 A2

L10: Entry 4 of 6

File: DWPI

Oct 16, 2000

DERWENT-ACC-NO: 2000-647235

DERWENT-WEEK: 200106

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TITLE: Novel nucleic acid encoding cullin regulating ring finger proteins, termed as ROC proteins similar to anaphase-promoting complex 11, for therapeutic and diagnostic use

INVENTOR: OHTA, T; XIONG, Y

PRIORITY-DATA: 1999US-0166927 (November 22, 1999), 1999US-0127261 (March 31, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 200040569 A	October 16, 2000	N/A	000	C12N015/12
WO 200058472 A2	October 5, 2000	E	083	C12N015/12

INT-CL (IPC): C07K 16/18; C12N 15/11; C12N 15/12; C12Q 1/02; C12Q 1/68; G01N 33/68

ABSTRACTED-PUB-NO: WO 200058472A

BASIC-ABSTRACT:

NOVELTY - An isolated nucleic acid (I) encoding ring finger proteins, ROC1 and ROC2 comprising a 327 or 342 nucleotide sequence (S1), both fully defined in the specification, a sequence (S2) that hybridizes to S1 under stringent hybridization conditions and encodes ROC1 or ROC2, respectively, or a sequence that differ from S1 and S2 due to degeneracy of genetic code, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) an expression vector (II) comprising (I);
- (2) a cell (III) comprising (II);
- (3) an isolated protein, ROC1 or ROC2, encoded by (I);
- (4) an antibody (Ab) which specifically binds to ROC proteins;
- (5) an antisense oligonucleotide (Ia) complementary to (I) and long enough to hybridize with (I) under stringent hybridization conditions;
- (6) an expression vector (IIa) comprising (Ia);
- (7) a DNA encoding (Ia);
- (8) production (P) of ROC1 or ROC2, comprising culturing (III) under expression conditions, and recovering the polypeptide;
- (9) detecting (I) in a biological sample, by hybridizing the complement of (I) to nucleic acid material of the sample, and detecting the hybridization complex;
- (10) screening for a bioactive agent capable of binding to ROC protein, by combining ROC protein and a candidate bioactive agent, and determining their specific binding;
- (11) screening for a bioactive agent capable of interfering with the binding of ROC proteins and a cullin protein, by combining ROC protein, a candidate bioactive

agent and cullin protein, and determining the binding of ROC protein with cullin protein; and

(12) screening for a bioactive agent capable of modulating the activity of ROC protein, by combining ROC protein and a candidate bioactive agent, and determining the effect of the agent on the activity of protein, or by contacting candidate bioactive agent to a cell comprising a recombinant nucleic acid encoding ROC protein, and detecting the effect of agent on the cell.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Stimulator of cullin dependent ubiquitin ligase activity; regulator of CDK inhibitor Sic1 degradation by the SCF (undefined) pathway. No biological data is given.

USE - ROC proteins are useful for screening bioactive agents that interfere with the binding of ROC proteins with cullin proteins (Claimed). Pharmaceutical formulations comprising (I) and ROC proteins are useful for diagnostic and therapeutic purposes, preferably for diagnosing and treating tumors.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Draw Desc	Image
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☐ 5. Document ID: AU 9917744 A, WO 9934012 A1

L10: Entry 5 of 6

File: DWPI

Jul 19, 1999

DERWENT-ACC-NO: 1999-405517

DERWENT-WEEK: 199951

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TITLE: An assay for an inhibitor of eukaryotic cell cycle progression

INVENTOR: JOHNSTON, L H

PRIORITY-DATA: 1997GB-0027277 (December 23, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 9917744 A	July 19, 1999	N/A	000	C12Q001/02
WO 9934012 A1	July 8, 1999	E	045	C12Q001/02

INT-CL (IPC): C12Q 1/02

ABSTRACTED-PUB-NO: WO 9934012A

BASIC-ABSTRACT:

NOVELTY - An assay for modulators of the interaction between anaphase promoting complex protein (APC)-2, and other APC members, is new.

Yeast anaphase promoting complex (APC) component APC2 is new.

DETAILED DESCRIPTION - An assay for an inhibitor of eukaryotic cell cycle progression comprises:

(a) providing an APC2 protein, fragment or variant that is capable of associating with an APC;

(b) providing a second polypeptide member of the APC with which the APC2 is capable of forming a complex in the absence of a putative inhibitor;

(c) providing a putative inhibitor compound; and measuring the degree of inhibition of binding between (a) and (b) caused by the presence of the putative inhibitor.

USE - The method is useful for identifying inhibitors or modulators of cell cycle progression, particularly in fungal cells. The assay may also be used for other modulators of cell cycle progression, e.g. for compounds which enhance or stabilize the various interactions. Stabilization of the APC complex may also prevent or antagonize cell cycle progression, since the complex itself disassembles following the exit from mitosis.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Draw Desc	Image
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☐ 6. Document ID: JP 2001503987 W, EP 843008 A1, WO 9821326 A2, EP 942978 A2, MX 9904287 A1

L10: Entry 6 of 6

File: DWPI

Mar 27, 2001

DERWENT-ACC-NO: 1998-263286

DERWENT-WEEK: 200122

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TITLE: Identification of human anaphase-promoting complex subunits - and production of recombinant APC

INVENTOR: GALOVA, M; NASMYTH, K ; ZACHARIAE, W

PRIORITY-DATA: 1996EP-0118297 (November 14, 1996)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 2001503987 W	March 27, 2001	N/A	070	C12N015/09
EP 843008 A1	May 20, 1998	E	030	C12N015/12
WO 9821326 A2	May 22, 1998	E	000	C12N015/12
EP 942978 A2	September 22, 1999	E	000	C12N015/12
MX 9904287 A1	January 1, 2000	N/A	000	C12N015/12

INT-CL (IPC): C07K 14/47; C07K 16/18; C12N 15/09; C12N 15/12; C12P 21/02; C12P 21/08; C12Q 1/00; C12Q 1/68; G01N 33/15; G01N 33/50; G01N 33/53

ABSTRACTED-PUB-NO: EP 843008A

BASIC-ABSTRACT:

Identifying novel subunits of the human anaphase-promoting complex (APC) comprises replacing one or more endogenous genes encoding a known APC subunit in *Saccharomyces cerevisiae* cells with epitope-tagged versions of the genes or transforming the cells with a vector containing the corresponding epitope-tagged cDNAs, growing the yeast cells to prepare a protein extract, isolating the yeast APC by contacting the protein extract with an antibody directed against the epitope tag, isolating the antibody-bound proteins and purifying them, determining the sequence of the yeast proteins and identifying the human subunits by comparing the protein sequences or the DNA sequence encoding the proteins, with published human sequences. Also claimed are: (i) identifying novel subunits of the human APC by replacing one or more endogenous genes encoding known APC subunits in a human cell with epitope-tagged versions of the genes or transforming the cell with a vector containing the corresponding epitope-tagged cDNAs and establishing a cell line, growing the cell line and preparing a protein extract, isolating the APC by contacting the protein extract with an antibody directed against the epitope tag, isolating the antibody-bound proteins and purifying them and determining the sequence of the proteins; (ii) production of recombinant APC, in which cDNAs encoding APC subunits are expressed in a suitable host, and the subunits are isolated, purified and allowed to assemble into a functional APC.

USE - Recombinant APC is used in a screening method for identifying substances that inhibit rapidly proliferating cells by interfering with the cells' entry into the subsequent cell cycle. The screening method comprises determining the effect

the subsequent cell cycle. The screening method comprises determining the effect of a substance on the APC's ability to ubiquitinate a substrate which is of human origin, preferably recombinant cyclinB (all claimed).

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KMC	Draw Desc	Image
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USPT	11 same apc	3	L4
USPT	12 same recomb\$	2	L3
USPT	11 same ubiquitin	50	L2
USPT	cyclin same cycle	502	L1